CLAIMS

1. A method for suppressing the expression of a selected gene in a cell the method comprising introducing into the cell a molecule comprising (1) a nucleic acid binding portion which binds to a site at or associated with the selected gene which site is present in a genome and (2) an expression repressor portion, wherein the nucleic acid binding portion comprises an oligonucleotide or oligonucleotide mimic or analogue, and wherein the repressor portion comprises a polypeptide or peptidomimetic.

2. A method for modulating the expression of a selected gene in a cell the method comprising introducing into the cell a molecule comprising (1) a nucleic acid binding portion which binds to a site at or associated with the selected gene which site is present in a genome and (2) a modifying portion, wherein the nucleic acid binding portion comprises an oligonucleotide or oligonucleotide mimic or analogue, and wherein the modifying portion comprises a polypeptide or peptidomimetic which is capable of modulating covalent modification of nucleic acid or chromatin and is not an endonuclease.

3. The method of claim 1 or 2 wherein the repressor or modifying portion is a chromatin inactivation portion.

4. The method of claim 1 or 2 wherein the repressor or modifying portion is all or a portion of a component of a DNA methylase complex or all or a portion of a polypeptide which binds to or facilitates the recruitment of a DNA methylase complex.

5. The method of claim 1 or 2 wherein the repressor or modifying portion is all or a portion of a component of a histone acetyltransferase or all or a portion of a polypeptide which binds to or facilitates the recruitment of a histone acetyltransferase complex.

6. The method according to any one of the preceding claims wherein the polypeptide or peptidomimetic part of the molecule has a molecular mass of less than11 kDa.

7. A method according to any one of the preceding claims wherein the nucleic acid binding portion is a DNA binding portion.

8. A method according to any one of claims 1 to 6 wherein the nucleic acid binding portion is an RNA binding portion and the site present in a genome is a nascent RNA being transcribed from DNA.

9. The method of any of the preceding claims wherein the oligonucleotide or oligonucleotide analog or mimetic is a triplex forming oligonucleotide (TFO).

10. The method of any of the preceding claims wherein the oligonucleotide analog or mimetic is a peptide nucleic acid (PNA).

11. A method according to claim 3 or claims dependent thereon wherein the chromatin inactivation portion facilitates histone deacetylation.

12. A method according to claim 3 or claims dependent thereon or 11 wherein the chromatin inactivation portion is all or a portion of a component

of a histone deacetylation (HDAC) complex or all or a portion of a polypeptide which binds to or facilitates the recruitment of a HDAC complex.

13. A method according to Claim 12 wherein the component of the HDAC complex or the polypeptide which binds to or facilitates the recruitment of a HDAC complex is any one of PLZF, N-CoR, SMRT, Sin3, SAP18, SAP30, HDAC, NuRD, MAD1, MAD2, MAD3, MAD4, Rb or E7.

14. A method according to Claim 13 wherein the chromatin inactivation portion is all or a N-CoR- or SMRT-binding part of PLZF.

15. A method according to Claim 13 wherein the chromatin inactivation portion is all or an enzymatically active part of a HDAC.

16. A method according to claim 13 wherein the chromatin inactivation portion is all or a histone deacetylase complex-binding part of E7.

17. A method according to any of the preceding claims wherein the molecule further comprises a portion which facilitates cellular entry and/or nuclear localisation.

18. A method according to claim 18 wherein the portion which facilitates cellular entry and/or nuclear localisation is a small peptide of 7-16 amino acids, for example Modified Antennapedia homeodomain (RQIKIWFQNRRMKWKK) or basic HIV TAT internalisation peptide (C(Acm)GRKKRRQRRRPQC), where C(Acm) is a Cys-acetamidomethyl.

19. A method according to any one of Claims 1 to 18 wherein the nucleic acid binding portion and the repressor or modifying portion are fused.

20. A method according to any of the preceding claims wherein the cell is an eukaryotic cell.

21. A method according to any of the preceding claims wherein the cell is an animal cell and is contained within an animal or is a plant cell and is contained within a plant.

22. A method according to any of the preceding claims wherein the expression of a selected gene in a human is suppressed.

23. A method according to any of the preceding claims wherein the expression of a plurality of selected genes is suppressed.

24. Use of a molecule as defined in relation to any of the preceding claims in the manufacture of an agent for modulating the expression of the selected gene in a cell.

25. The use of claim 24 wherein the agent is for suppressing the expression of the selected gene.

26. Use according to Claim 24 or 25 wherein the agent is a medicament for modulating or suppressing the expression of a selected gene in an animal.

27. A method of treating a patient in need of suppression or modulation of the expression of a selected gene, the method comprising administering to the patient an effective amount of a molecule as defined in any of the previous claims.

28. Use of a molecule as defined in any of the previous claims in the manufacture of a medicament for suppressing the expression of a selected gene in a patient in need of such suppression.

29. A molecule as defined in any of the previous claims.

30. A molecule as defined in any of the previous claims for use in medicine.

31. A pharmaceutical composition comprising a molecule as defined in any of the previous claims and a pharmaceutically acceptable carrier.

32. The composition of claim 31 comprising means for promoting cellular uptake of the molecule, for example liposomes or a viral carrier.

33. A host cell comprising a molecule as defined in any one of the preceding claims.

34. A host cell according to Claim 33 which is a bacterial cell.

35. A host cell according to Claim 33 which is an animal cell.

36. A host cell according to Claim 33 which is a plant cell.

37. An animal comprising a host cell according to Claim 35.

38. A plant comprising a host cell according to Claim 36.

39. A method for designing a molecule for suppressing expression of a selected gene in a cell, the method comprising

(1) identifying a site at or associated with the selected gene

(2) identifying or designing a nucleic acid binding portion which binds to, or is predicted to bind to, the site (or a polynucleotide having or comprising the nucleotide sequence of the site)

(3) preparing a molecule comprising the nucleic acid binding portion and an expression repressor portion,

wherein the nucleic acid binding portion comprises an oligonucleotide or oligonucleotide mimic or analogue, and wherein the repressor portion comprises a polypeptide or peptidomimetic.

40. A method for designing a molecule for modulating expression of a selected gene in a cell, the method comprising

(1) identifying a site at or associated with the selected gene

(2) identifying or designing a nucleic acid binding portion which binds to, or is predicted to bind to, the site (or a polynucleotide having or comprising the nucleotide sequence of the site)

(3) preparing a molecule comprising the nucleic acid binding portion and a modifying portion,

wherein the nucleic acid binding portion comprises an oligonucleotide or oligonucleotide mimic or analogue, and wherein the modifying portion

comprises a polypeptide or peptidomimetic which is capable of modulating covalent modification of nucleic acid or chromatin.

41. The method of claim 39 or 40 further comprising the steps of

(4) performing a quality control assessment on the molecule preparation in order to determine that the nucleic acid binding portion and repressor or modifying portion are attached to each other; and/or

(5) testing the affinity and/or specificity of binding of the nucleic acid binding portion to the site and/or a polynucleotide having or comprising the nucleotide sequence of the site; and/or

(6) testing the affinity and/or specificity of binding of the molecule to the site and/or a polynucleotide having or comprising the nucleotide sequence of the site; and/or

(7) testing the efficacy of the molecule or polynucleotide in modulating or suppressing the expression of the gene and/or of a reporter gene comprising the nucleotide sequence of the site.

42. Any novel method of modulating, for example suppressing, the activity of a selected gene in a cell, for example plant or animal cell, as herein described.

43. Any novel molecule which modulates, for example suppresses, the activity of a selected gene in a cell, for example plant or animal cell, as herein described.

The nucleic acid binding portion may be a triplex forming oligonucleotide (TFO).

Figure 1